

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
7 August 2003 (07.08.2003)

PCT

(10) International Publication Number  
**WO 2003/064626 A3**

- (51) International Patent Classification<sup>7</sup>: **C07H 21/04**, C12N 15/00
- (21) International Application Number:  
PCT/US2003/003223
- (22) International Filing Date: 3 February 2003 (03.02.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/353,203 1 February 2002 (01.02.2002) US  
60/353,381 1 February 2002 (01.02.2002) US  
60/436,238 23 December 2002 (23.12.2002) US  
60/438,608 7 January 2003 (07.01.2003) US
- (71) Applicant: SEQUITUR, INC. [US/US]; 14 Tech Circle, Natick, MA 01760 (US).
- (72) Inventors: WOOLF, Tod, M.; 17 Pheasant Avenue, Sudbury, MA 01776 (US). WIEDERHOLT, Kristin, A.; 2 Shay Road, Hudson, MA 01749 (US).
- (74) Agents: WARBURG, Richard, J. et al.; FOLEY & LARDNER, P.O. Box 80278, San Diego, CA 92138-0278 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— with international search report  
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report:  
10 June 2004
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2003/064626 A3

(54) Title: DOUBLE-STRANDED OLIGONUCLEOTIDES

(57) Abstract: Antisense sequences, including duplex RNAi compositions, which possess improved properties over those taught in the prior art are disclosed. The invention provides optimized antisense oligomer compositions and method for making and using the both in *in vitro* systems and therapeutically. The invention also provides methods of making and using the improved antisense oligomer compositions.

BEST AVAILABLE COPY

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/03223

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : C07H 21/04; C12N 15/00

US CL : 536/24.1, 24.5

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/24.1, 24.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
WEST, CAPLUS, EMBASE, BIOTECHNO, MEDLINE**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ASHLEY et al., Chemical Synthesis of Oligodeoxynucleotide Dumbbells. Biochemistry. 1991, Vol. 30, pages 2927-2933, see entire document.	1-4, 14, 15
---		-----
Y		5-13, 16-23
Y	GIOVANNANGELI et al., Oligonucleotide Clamps Arrest DNA synthesis on a single-Stranded DNA Target. Proc. Natl. Acad. Sci. November 1993, Vol. 90, pages 10013-10017, see entire document.	1-23
Y	CHU et al., The Stability of Different Forms of Double-Stranded Decoy DNA in Serum and Nuclear Extracts, nucleic Acids Research, 1992, Vol. 20, No. 21, pages 5857-5858,	1-23
Y	YAMAKAWA et al., Properties and Anti-HIV Activity of Nicked Dumbbell Oligonucleotides. Nucleosides & Nucleotides. 1996, Vol. 15, Nos. 1-3, pages 519-529, see entire document.	1-23
Y	US 6,048,974 A (GRYAZNOV et al) 11 April 2000 (11.04.2000), see entire document.	1-23
Y	US 6,133,024 (HELENE et al) 17 October 2000 (17.10.2000), see entire document.	1-23

☒ Further documents are listed in the continuation of Box C.☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&amp;"

document member of the same patent family

Date of the actual completion of the international search

29 October 2003 (29.10.2003)

Date of mailing of the international search report

03 MAY 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US

Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

Facsimile No. (703)305-3230

Authorized officer

Sean R McGarry

Telephone No. (703) 308-0196

BEST AVAILABLE COPY